

We Claim:

1. A method of selectively inhibiting the growth of a malignant cell in a mammal, comprising:
delivering to a malignant cell in a mammal an HSV-1-derived viral vector containing a DNA having a deletion in both copies of the LAT gene and a deletion in both copies of the ICP34.5 gene of HSV-1; and
causing said cell to internalize and express said vector, transcripts encoding LAT gene product and ICP34.5 gene product not being detectably produced in said malignant cell, whereby inhibition of the growth of said malignant cell results.
2. The method of Claim 1, wherein said malignant cell is derived from or is contained in a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, lymphoma, or carcinoma.
3. The method of Claim 1, wherein the malignant cell is contained in a malignancy in the skull, brain, spine, thorax, lung, peritoneum, prostate, ovary, uterus, breast, stomach, liver, bowel, colon, rectum, bone, lymphatic system, or skin, of said mammal.
4. The method of Claim 1, wherein said mammal is a human, non-human primate, mouse, rat, gerbil, hamster, or rabbit.
5. The method of Claim 1, wherein said HSV-1-derived vector is derived from HSV-1 strain McKrae.
6. The method of Claim 1, wherein the HSV-1-derived vector is Δ LAT Δ 34.5 or Prom Δ LAT Δ 34.5, or a derivative of either of these.
7. The method of Claim 1, wherein said HSV-1-derived vector is delivered by intrathecal injection.
8. The method of Claim 1, wherein said malignant cell is contained in a

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tumor, and said HSV-1-derived vector is delivered by an intratumoral injection to the malignant cell via a surgical incision.

9. The method of Claim 8, wherein the surgical incision is a craniotomy.

10. The method of Claim 8, further comprising surgically debulking the tumor containing the malignant cell before delivering said HSV-1-derived vector.

11. The method of Claim 1, wherein said HSV-1-derived vector is delivered by stereotactic inoculation.

12. The method of Claim 1, wherein said HSV-1-derived vector is delivered transvascularly.

13. The method of Claim 12, wherein transvascular delivery is by intravenous or intra-arterial injection.

14. The method of Claim 13, further comprising disrupting the blood-brain barrier before or substantially simultaneously with intra-arterial injection of said HSV-derived vector, whereby passage of said HSV-1-derived vector across the blood-brain barrier is facilitated.

15. The method of Claim 14, wherein disruption of the blood-brain barrier is accomplished by administering to the mammal a hypertonic infusion.

16. The method of Claim 15, wherein the hypertonic infusion is a mannitol infusion.

17. The method of Claim 13, further comprising administering to said mammal a vasoactive agent before or substantially simultaneously with intra-arterial injection of said HSV-derived vector, whereby passage of said HSV-1-derived vector across the blood-brain barrier is facilitated.

18. The method of Claim 17, wherein said vasoactive agent is bradykinin or a functional analog thereof.

19. A method of selectively inhibiting the growth of a malignant cell in a mammal, comprising:

5 delivering to a malignant cell in a mammal an HSV-1-derived vector containing a DNA having a deletion in both copies of the LAT gene and a deletion in both copies of the ICP34.5 gene of HSV-1, the DNA of said vector comprising at least one transcriptional unit of a LAT promoter sequence or operative fragment thereof, operatively linked to a nucleic acid sequence encoding a protein, or functional fragment thereof, toxic to said malignant cell; and

10 causing said cell to internalize said vector and express, from said transcriptional unit, transcript encoding said toxic protein, or functional fragment thereof, transcripts encoding LAT gene product and ICP34.5 gene product not being detectably produced in said malignant cell, whereby said toxic protein, or functional fragment thereof, is produced in said malignant cell, resulting in an inhibition of the growth of said malignant cell.

20. The method of Claim 19, wherein said malignant cell is derived from or is contained in a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, lymphoma, or carcinoma.

21. The method of Claim 19, wherein the malignant cell is contained in a malignancy in the skull, brain, spine, thorax, lung, peritoneum, prostate, ovary, uterus, breast, stomach, liver, bowel, colon, rectum, bone, lymphatic system, or skin, of said mammal.

22. The method of Claim 19, wherein said mammal is a human, non-human primate, mouse, rat, gerbil, hamster, or rabbit.

23. The method of Claim 19, wherein said HSV-1-derived vector is derived from HSV-1 strain McKrae.

24. The method of Claim 19, wherein the HSV-1-derived vector is Δ LAT Δ 34.5 or Prom Δ LAT Δ 34.5, or a derivative of either of these.

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25. The method of Claim 19, wherein said HSV-1-derived vector is delivered by intrathecal injection.

26. The method of Claim 19, wherein said malignant cell is contained in a tumor, and said HSV-1-derived vector is delivered by an intratumoral injection to the malignant cell via a surgical incision.

27. The method of Claim 26, wherein the surgical incision is a craniotomy.

28. The method of Claim 26, further comprising surgically debulking the tumor containing the malignant cell before delivering said HSV-1-derived vector.

29. The method of Claim 19, wherein said HSV-1-derived vector is delivered by stereotactic inoculation.

30. The method of Claim 19, wherein said HSV-1-derived vector is delivered transvascularily.

31. The method of Claim 30, wherein transvascular delivery is by intravenous or intra-arterial injection.

32. The method of Claim 31, further comprising disrupting the blood-brain barrier before or substantially simultaneously with intra-arterial injection of said HSV-derived vector, whereby passage of said HSV-1-derived vector across the blood-brain barrier is facilitated.

33. The method of Claim 32, wherein disruption of the blood-brain barrier is accomplished by administering to the mammal a hypertonic infusion.

34. The method of Claim 33, wherein the hypertonic infusion is a mannitol infusion.

35. The method of Claim 31, further comprising administering to said mammal a vasoactive agent before or substantially simultaneously with intra-arterial injection of said HSV-derived vector,

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whereby passage of said HSV-1-derived vector across the blood-brain barrier is facilitated.

36. The method of Claim 35, wherein said vasoactive agent is bradykinin or a functional analog thereof.

37. The method of Claim 19, wherein said toxic protein is human interferon- γ , interleukin-2, interleukin-4, interleukin-6, interleukin-10, interleukin-12, granulocyte-macrophage colony stimulating factor, tumor necrosis factor- α , Fas ligand, human connexin-43, VP-16, or VP-22, or a functional fragment or fusion protein derived from any of these.

38. A method of selectively inhibiting the growth of a malignant cell in a mammal, comprising:

delivering to a malignant cell in a mammal an HSV-1-derived vector containing a DNA having a deletion in both copies of the LAT gene and a deletion in both copies of the ICP34.5 gene of HSV-1, the DNA of said vector comprising at least one transcriptional unit of a LAT promoter sequence or operative fragment thereof, operatively linked to a nucleic acid sequence encoding a human interferon- γ , interleukin-2, interleukin-4, interleukin-6, interleukin-10, interleukin-12, granulocyte-macrophage colony stimulating factor, tumor necrosis factor- α , Fas ligand, human connexin-43, VP-16, or VP-22, or a functional fragment or fusion protein derived from any of these; and

causing said cell to internalize said vector and express transcript from said transcriptional unit, transcripts encoding LAT gene product and ICP34.5 gene product not being detectably produced in said malignant cell, whereby human interferon- γ , interleukin-2, interleukin-4, interleukin-6, interleukin-10, interleukin-12, granulocyte-macrophage colony stimulating factor, tumor necrosis factor- α , Fas ligand, human connexin-43, VP-16, VP-22, or a functional fragment or fusion protein derived from any of these, is produced, resulting in an inhibition of the growth of said malignant cell.

39. The method of Claim 38, wherein said malignant cell is derived from or is contained in a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, lymphoma, or carcinoma.

40. The method of Claim 38, wherein the malignant cell is contained in a malignancy

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in the skull, brain, spine, thorax, lung, peritoneum, prostate, ovary, uterus, breast, stomach, liver, bowel, colon, rectum, bone, lymphatic system, or skin, of said mammal.

41. The method of Claim 38, wherein said mammal is a human, non-human primate,
5 mouse, rat, gerbil, hamster, or rabbit.

42. The method of Claim 38, wherein said HSV-1-derived vector is derived
from HSV-1 strain McKrae.

10 43. The method of Claim 38, wherein the HSV-1-derived vector is Δ LAT Δ 34.5
or Prom Δ LAT Δ 34.5, or a derivative of either of these.

44. The method of Claim 38, wherein said malignant cell is contained in a
tumor, and said HSV-1-derived expression vector is delivered by an intratumoral injection to the
malignant cell via a surgical incision.

45. The method of Claim 44, wherein the surgical incision is a craniotomy.

46. The method of Claim 44, further comprising surgically debulking the tumor containing
the malignant cell before delivering said HSV-1-derived vector.

47. The method of Claim 38, wherein said HSV-1-derived vector is delivered by
stereotactic inoculation.

25 48. The method of Claim 38, wherein said HSV-1-derived vector is delivered
transvascularily.

49. The method of Claim 48, wherein transvascular delivery is by intra-arterial
injection.

30 50. The method of Claim 49, further comprising disrupting the blood-brain barrier before
or substantially simultaneously with intra-arterial injection of said HSV-derived vector, whereby passage

of said HSV-1-derived vector across the blood-brain barrier is facilitated.

51. The method of Claim 50, wherein disruption of the blood-brain barrier accomplished by administering to the mammal a hypertonic infusion.

52. The method of Claim 51, wherein the hypertonic infusion is a mannitol infusion.

53. The method of Claim 49, further comprising administering to said mammal a vasoactive agent before or substantially simultaneously with intra-arterial injection of said HSV-derived vector, whereby passage of said HSV-1-derived vector across the blood-brain barrier is facilitated.

54. The method of Claim 53, wherein said vasoactive agent is bradykinin or a functional analog thereof.

55. A method of selectively inhibiting the growth of a malignant cell in a mammal, comprising:

delivering to a malignant cell in a mammal an HSV-1-derived vector containing a DNA having a deletion in both copies of the LAT gene and a deletion in both copies of the ICP34.5 gene of HSV-1, said vector, having a functional HSV thymidine kinase gene;

causing said malignant cell to internalize said vector and express transcripts encoding HSV thymidine kinase, whereby HSV thymidine kinase is produced in said malignant cell, and transcripts encoding LAT gene product and ICP34.5 gene product are not detectably produced in said malignant cell; and

administering to said mammal a dose of gancyclovir or acyclovir, whereby gancyclovir or acyclovir is converted by HSV thymidine kinase to a nucleotide analog within said malignant cell, and whereby the growth of said malignant cell is inhibited.

56. The method of Claim 55, wherein said malignant cell is derived from or is contained in a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, lymphoma, or carcinoma.

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57. The method of Claim 55, wherein the malignant cell is contained in a malignancy in the skull, brain, spine, thorax, lung, peritoneum, prostate, ovary, uterus, breast, stomach, liver, bowel, colon, rectum, bone, lymphatic system, or skin, of said mammal.

5 58. The method of Claim 55, wherein said mammal is a human, non-human primate, mouse, rat, gerbil, hamster, or rabbit.

59. The method of Claim 55, wherein said HSV-1-derived vector is derived from HSV-1 strain McKrae.

10 60. The method of Claim 55, wherein the HSV-1-derived vector is Δ LAT Δ 34.5 or Prom Δ LAT Δ 34.5, or a derivative of either of these.

61. The method of Claim 55, wherein said malignant cell is contained in a tumor, and said HSV-1-derived vector is delivered by an intratumoral injection to the malignant cell via a surgical incision.

62. The method of Claim 61, wherein the surgical incision is a craniotomy.

63. The method of Claim 61, further comprising surgically debulking the tumor containing the malignant cell before delivering said HSV-1-derived expression vector.

64. The method of Claim 55, wherein said HSV-1-derived expression vector is delivered by stereotactic inoculation.

25 65. The method of Claim 55, wherein said HSV-1-derived expression vector is delivered transvascularly.

30 66. The method of Claim 65, wherein transvascular delivery is by intravenous or intra-arterial injection.

67. The method of Claim 66, further comprising disrupting the blood-brain barrier before

or substantially simultaneously with intra-arterial injection of said HSV-derived vector, whereby passage of said HSV-1-derived vector across the blood-brain barrier is facilitated.

68. The method of Claim 67, wherein disruption of the blood-brain barrier accomplished by administering to the mammal a hypertonic infusion.

69. The method of Claim 68, wherein the hypertonic infusion is a mannitol infusion.

70. The method of Claim 66, further comprising administering to said mammal a vasoactive agent before or substantially simultaneously with intra-arterial injection of said HSV-derived vector, whereby passage of said HSV-1-derived vector across the blood-brain barrier is facilitated.

71. The method of Claim 70, wherein said vasoactive agent is bradykinin or a functional analog thereof.

72. A method of expressing in a mammalian cell a gene encoding a preselected protein, comprising:

delivering to a mammalian cell an HSV-1-derived vector containing a DNA having a deletion in both copies of the LAT gene and a deletion in both copies of the ICP34.5 gene of HSV-1, the DNA of said vector comprising at least one transcriptional unit of a LAT promoter sequence or operative fragment thereof, operatively linked to a nucleic acid sequence encoding a preselected protein; and

causing said cell to internalize said vector and express transcript encoding said preselected protein from said transcriptional unit, transcripts encoding LAT gene product and ICP34.5 gene product not being detectably produced in said cell, said preselected protein being produced in said cell, whereby said HSV-expressing cell produces an elevated amount of said desired protein compared to a homologous uninfected cell.

73. The method of Claim 72, wherein said cell is a malignant cell.

74. The method of Claim 72, wherein said cell is a non-malignant cell.

75. The method of Claim 72, wherein said cell is a malignant cell derived from or is

contained in a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, lymphoma, or carcinoma.

5 76. The method of Claim 72, wherein the malignant cell is derived from or is contained in

a malignancy in the skull, brain, spine, thorax, lung, peritoneum, prostate, ovary, uterus, breast, stomach, liver, bowel, colon, rectum, bone, lymphatic system, or skin, of a mammal.

10 77. The method of Claim 72, wherein said mammalian cell is derived from or is contained

in a human, non-human primate, mouse, rat, gerbil, hamster, or rabbit.

 78. The method of Claim 72, wherein said HSV-1-derived vector is derived from HSV-1 strain McKrae.

 79. The method of Claim 72, wherein the HSV-1-derived vector is Prom Δ LAT Δ 34.5, or a derivative thereof.

 80. The method of Claim 72, wherein the preselected protein is a fluorescent or light-emitting protein or a cytokine.

25 81. The method of Claim 80, wherein said fluorescent or light-emitting protein is a green fluorescent protein, yellow fluorescent protein, blue fluorescent protein, phycobiliprotein, luciferase, or apoaequorin.

30 82. The method of Claim 72, further comprising introducing said HSV-1-derived vector to a mammalian cell in vitro.

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83. The method of Claim 72, further comprising introducing said HSV-1-derived vector to the mammalian cell within a mammal in vivo.
84. The method of Claim 83, wherein said mammal is a human, non-human primate, mouse, rat, gerbil, hamster, or rabbit.
85. The method of Claim 83, wherein said mammalian cell is a malignant cell contained in a tumor, and said HSV-1-derived expression vector is delivered by an intratumoral injection to the malignant cell via a surgical incision.
86. The method of Claim 83, wherein the surgical incision is a craniotomy.
87. The method of Claim 85, further comprising surgically debulking the tumor containing the cell before delivering said HSV-1-derived expression vector.
88. The method of Claim 83, wherein said HSV-1-derived vector is delivered by stereotactic inoculation.
89. The method of Claim 83, wherein said HSV-1-derived vector is delivered transvascularly.
90. The method of Claim 89, wherein transvascular delivery is by intra-arterial injection.
91. The method of Claim 90, further comprising disrupting the blood-brain barrier before or substantially simultaneously with intra-arterial injection of said HSV-derived vector, whereby passage of said HSV-1-derived vector across the blood-brain barrier is facilitated.
92. The method of Claim 91, wherein disruption of the blood-brain barrier is accomplished by administering to the mammal a hypertonic infusion.
93. The method of Claim 92, wherein the hypertonic infusion is a mannitol infusion.

94. The method of Claim 90, further comprising administering to said mammal a vasoactive agent before or substantially simultaneously with intra-arterial injection of said HSV-derived vector, whereby passage of said HSV-1-derived vector across the blood-brain barrier is facilitated.

95. The method of Claim 94, wherein said vasoactive agent is bradykinin or a functional analog of bradykinin.

96. A method of treating a genetic defect in a mammal, comprising the method of Claim 72.

97. A method of detecting the presence of a cell expressing HSV-1, comprising:
delivering to a mammalian cell an HSV-1-derived vector containing DNA having a deletion in both copies of the LAT gene and a deletion in both copies of the ICP34.5 gene of HSV-1, the DNA of said vector comprising at least one transcriptional unit of a LAT promoter sequence or operative fragment thereof, operatively linked to a nucleic acid sequence encoding a fluorescent or light-emitting protein; and

causing said cell to internalize said vector and express transcript from said transcriptional unit, transcripts encoding LAT gene product and ICP34.5 gene product not being detectably produced in said cell, said fluorescent or light-emitting protein being produced in said cell, whereby said HSV-expressing cell is detected via luminescence or fluorescence therefrom.

98. The method of Claim 97, wherein said cell is a malignant cell.

99. The method of Claim 97, wherein said cell is a non-malignant cell.

100. The method of Claim 97, wherein said cell is a malignant cell derived from or contained in a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, lymphoma, or carcinoma.

101. The method of Claim 97, wherein the cell is derived from or is contained in a malignancy in the skull, brain, spine, thorax, lung, peritoneum, prostate, ovary, uterus, breast, stomach,

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liver, bowel, colon, rectum, bone, lymphatic system, or skin, of a mammal.

102. The method of Claim 97, wherein said mammalian cell is derived from or is contained in a human, non-human primate, mouse, rat, gerbil, hamster, or rabbit.

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103. The method of Claim 97, wherein said HSV-1-derived vector is derived from HSV-1 strain McKrae.

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104. The method of Claim 97, wherein the HSV-1-derived vector is Prom Δ LAT Δ 34.5, or a derivative thereof.

105. The method of Claim 97, wherein said fluorescent or light-emitting protein is a green fluorescent protein, yellow fluorescent protein, blue fluorescent protein, phycobiliprotein, luciferase, or apoaquorin.

106. The method of Claim 97, further comprising introducing said HSV-1-derived vector to a mammalian cell in vitro.

107. The method of Claim 97, further comprising introducing said HSV-1-derived vector to the mammalian cell within a mammal in vivo.

108. The method of Claim 107, wherein said mammal is a human, non-human primate, mouse, rat, gerbil, hamster, or rabbit.

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109. The method of Claim 107, wherein said cell is a malignant cell contained in a tumor, and said HSV-1-derived vector is delivered by an intratumoral injection to the malignant cell via a surgical incision.

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110. The method of Claim 109, wherein the surgical incision is a craniotomy.

111. The method of Claim 109, further comprising surgically debulking the tumor containing

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the cell before delivering said HSV-1-derived vector.

112. The method of Claim 107, wherein said HSV-1-derived vector is delivered by stereotactic inoculation.

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113. The method of Claim 107, wherein said HSV-1-derived vector is delivered transvascularily.

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114. The method of Claim 113, wherein transvascular delivery is by intra-arterial injection.

115. The method of Claim 114, further comprising disrupting the blood-brain barrier before or substantially simultaneously with intra-arterial injection of said HSV-derived vector, whereby passage of said HSV-1-derived vector across the blood-brain barrier is facilitated.

116. The method of Claim 115, wherein disruption of the blood-brain barrier is accomplished by administering to the mammal a hypertonic infusion.

117. The method of Claim 116, wherein the hypertonic infusion is a mannitol infusion.

118. The method of Claim 114, further comprising administering to said mammal a vasoactive agent before or substantially simultaneously with intra-arterial injection of said HSV-derived vector, whereby passage of said HSV-1-derived vector across the blood-brain barrier is facilitated.

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119. The method of Claim 118, wherein said vasoactive agent is bradykinin or a functional analog thereof.

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120. An HSV-1-derived vector, having a functional HSV thymidine kinase gene, a deletion in both copies of the HSV-1 LAT gene, and a deletion in both copies of the HSV ICP34.5 gene, such that functional RNA transcripts encoding the LAT gene product and encoding the ICP34.5 gene product cannot be detected within a mammalian cell hosting said vector.

121. The HSV-derived vector of Claim 120, wherein said HSV-1-derived expression vector is derived from HSV-1 strain McKrae.

122. The HSV-1-derived vector of Claim 121, wherein the HSV-1-derived vector is Δ LAT Δ 34.5, Prom Δ LAT Δ 34.5, Prom Δ LAT Δ 34.5-GFP, or a derivative of any of these.

123. The HSV-1-derived vector of Claim 120, further comprising a DNA having at least one nucleic acid sequence defining a functional LAT promoter.

124. The HSV-1-derived vector of Claim 120, further comprising a DNA having at least one transcriptional unit having a functional LAT Promoter sequence or operative fragment thereof, operatively linked to nucleic acid encoding a preselected protein.

125. The HSV-1-derived vector of Claim 124, wherein the preselected protein is a fluorescent or light-emitting protein.

126. The HSV-1-derived vector of Claim 125, wherein said fluorescent or light-emitting protein is a green fluorescent protein, yellow fluorescent protein, blue fluorescent protein, phycobiliprotein, luciferase, or apoaequorin.

127. The HSV-1-derived vector of Claim 126, wherein the vector is Prom Δ LAT Δ 34.5-GFP or a derivative thereof.

128. The HSV-1-derived vector of Claim 123, wherein the HSV-1-derived vector is Prom Δ LAT Δ 34.5, Prom Δ LAT Δ 34.5-GFP, or a derivative of either of these.

129. The HSV-1-derived vector of Claim 124, wherein the preselected protein is a protein toxic to cells expressing HSV.

130. The HSV-1-derived vector of Claim 124, wherein the preselected protein is human interferon- γ , interleukin-2, interleukin-4, interleukin-6, interleukin-10, interleukin-12,

granulocyte-macrophage colony stimulating factor, tumor necrosis factor- α , Fas ligand, human connexin-43, VP-16, or VP-22, or a fusion protein derived from any of these.

131. An HSV-1-derived vector, comprising a DNA having at least one nucleic acid sequence defining a functional LAT promoter sequence or operative fragment thereof, and having a deletion in both copies of the HSV-1 LAT gene and a deletion in both copies of the HSV ICP34.5 gene, such that functional RNA transcripts encoding the LAT gene product and encoding the ICP34.5 gene product cannot be detected within a mammalian cell hosting said vector.

132. The HSV-1-derived vector of Claim 131, wherein said HSV-1-derived vector is derived from HSV-1 strain McKrae.

133. The HSV-1-derived vector of Claim 131, further comprising a functional HSV thymidine kinase gene.

134. The HSV-1-derived vector of Claim 132, wherein the HSV-1-derived vector is Prom Δ LAT Δ 34.5, Prom Δ LAT Δ 34.5-GFP, or a derivative of either of these.

135. The HSV-1-derived vector of Claim 131, further comprising a DNA having at least one transcriptional unit having a LAT Promoter sequence or operative fragment thereof, operatively linked to a nucleic acid encoding a preselected protein.

136. The HSV-1-derived vector of Claim 135, wherein the preselected protein is a fluorescent or light-emitting protein or cytokine.

137. The HSV-1-derived vector of Claim 136, wherein said fluorescent or light-emitting protein is a green fluorescent protein, yellow fluorescent protein, blue fluorescent protein, phycobiliprotein, luciferase, or apoaquorin.

138. The HSV-1-derived vector of Claim 137, wherein the vector is Prom Δ LAT Δ 34.5-GFP or a derivative thereof.

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139. The HSV-1-derived vector of Claim 131, wherein the preselected protein is a protein toxic to a cell expressing HSV.

140. The HSV-1-derived vector of Claim 131, wherein the preselected protein is human interferon- γ , interleukin-2, interleukin-4, interleukin-6, interleukin-10, interleukin-12, granulocyte-macrophage colony stimulating factor, tumor necrosis factor- α , Fas ligand, human connexin-43, VP-16, or VP-22, or a functional fragment or fusion protein derived from any of these.

141. A mammalian cell containing an HSV-1-derived vector selected from the group consisting of Δ LAT Δ 34.5, Prom Δ LAT Δ 34.5, and Prom Δ LAT Δ 34.5-GFP, or containing a derivative or unpackaged DNA of any of these.

142. The mammalian cell of Claim 141, wherein said cell is a malignant cell.

143. The mammalian cell of Claim 141, wherein said cell is a non-malignant cell.

144. The mammalian cell of Claim 141, wherein said cell is a malignant cell derived from or is contained in a glioma, glioblastoma, oligodendroglioma, astrocytoma, ependymoma, primitive neuroectodermal tumor, atypical meningioma, malignant meningioma, neuroblastoma, sarcoma, lymphoma, or carcinoma.

145. The mammalian cell of Claim 141, wherein said mammalian cell is derived from or is contained in a human, non-human primate, mouse, rat, gerbil, hamster, or rabbit.

146. A mammalian cell containing the HSV-1-derived vector of Claim 120 or unpackaged DNA thereof.

147. A mammalian cell containing the HSV-1-derived vector of Claim 121 or unpackaged DNA thereof.

148. A mammalian cell containing the HSV-1-derived vector of Claim 123 or unpackaged

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DNA thereof.

149. A mammalian cell containing the HSV-1-derived vector of Claim 124 or unpackaged DNA thereof.

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150. A mammalian cell containing the HSV-1-derived vector of Claim 125 or unpackaged DNA thereof.

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151. A mammalian cell containing the HSV-1-derived vector of Claim 126 or unpackaged DNA thereof.

152. A mammalian cell containing the HSV-1-derived vector of Claim 129 or unpackaged DNA thereof.

153. A mammalian cell containing the HSV-1-derived vector of Claim 130 or unpackaged DNA thereof.

154. A mammalian cell containing the HSV-1-derived vector of Claim 131 or unpackaged DNA thereof.

155. A mammalian cell containing the HSV-1-derived vector of Claim 132 or unpackaged DNA thereof.

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156. A mammalian cell containing the HSV-1-derived vector of Claim 133 or unpackaged DNA thereof.

157. A mammalian cell containing the HSV-1-derived vector of Claim 135 or unpackaged DNA thereof.

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158. A mammalian cell containing the HSV-1-derived vector of Claim 136 or unpackaged

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DNA thereof.

159. A mammalian cell containing the HSV-1-derived vector of Claim 137 or unpackaged DNA thereof.

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160. A mammalian cell containing the HSV-1-derived vector of Claim 139 or unpackaged DNA thereof.

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161. A mammalian cell containing the HSV-1-derived vector of Claim 140 or unpackaged DNA thereof.

162. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing an HSV-1-derived vector selected from the group consisting of Δ LAT Δ 34.5, Prom Δ LAT Δ 34.5, and Prom Δ LAT Δ 34.5-GFP, or containing a derivative of any of these.

163. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 120.

164. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 121.

165. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 122.

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166. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 124.

167. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 125.

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168. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 126.

5 169. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 129.

170. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 130.

10 171. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 131.

172. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 132.

173. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 133.

174. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 135.

175. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 136.

25 176. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 137.

177. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 139.

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178. A kit for expressing in a mammalian cell a gene encoding a preselected protein, containing the HSV-1-derived vector of Claim 140.

5 179. The method of Claim 1, wherein a bispecific antibody is used to cause said cell to internalize said vector.

180. The method of Claim 19, wherein a bispecific antibody is used to cause said cell to internalize said vector.

10 181. The method of Claim 38, wherein a bispecific antibody is used to cause said cell to internalize said vector.

182. The method of Claim 55, wherein a bispecific antibody is used to cause said cell to internalize said vector.

183. The method of Claim 72, wherein a bispecific antibody is used to cause said cell to internalize said vector.

184. The method of Claim 97, wherein a bispecific antibody is used to cause said cell to internalize said vector.

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